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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/271,098	03/18/99	CHERN	R 20023Y

000210
MERCK AND CO INC
P O BOX 2000
RAHWAY NJ 07065-0907

HM22/0424

EXAMINER	
SHAREEH S	
ART UNIT	**PAPER NUMBER**
1616	9

DATE MAILED: 04/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/271,098	Chern et al
Examiner	**Group Art Unit**
Shahnam Sharareh	1616

☒ Responsive to communication(s) filed on *Jan 14, 100*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-14* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-14* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Amendment filed on February 23, 2000 has been entered. Accordingly claims 1-11, 13 have been amended. Claims 1-14 are now pending.

Information Disclosure Statement

1. Applicant is hereby informed that the previously missing foreing patents; EP 0 179 022, EP 0 508 699, EP 0 846 686, EP 0 295 117, EP 0 892 060, EP 0 007 812, EP 0 002 916, and WO 96/29073, were recieved upon special package delivery to the Examiner. Since no PTO Form-1449 was submitted with the instant package, Examiner has cited the delivered references in PTO Form 892 to indicate the consideration of said references.

Response to Arguments

2. The rejection of claims 1-3, 5-6, 11-13 made under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office Action filed on November 10, 99 is withdrawn in view of the newly amended claims.

3. Applicant's arguments in respect to the rejection of claims 1-6, 8-11, 13, made under 35 U.S.C. 102(b) as being anticipated by Dunn et al US Patent 5,278,202 were found persuasive. Thus, said rejection is withdrawn.

4. Applicant's arguments filed on February 23, 2000 in respect to the rejection made under 35 U.S.C. 102(e) as being anticipated by Yewey et al US Patent 5,780,044 has been considered and were found persuasive. Said rejection is withdrawn.

5. Applicant's arguments filed on February 23, 2000 in respect to the rejection made under 35 U.S.C. 102(e) as being anticipated by by Lewis US Patent 5,733,566 has been considered, but were not found persuasive.

The traversal is on the basis that Lewis forms "microparticles that serve as a matrix from which the active agent is dispersed." and further that Lewis does not disclose a composition that forms a film encapsulated liquid *in situ*. In response, Examiner draws Applicant's attention to the recitation of the independent claims in this case claim 1. Accordingly, the instant claim is directed to liquid polymeric compositions comprising (a) 1 to 30% w/v of a hydrophobic bioactive substance , (b) 1 to 20% w/v of a poly(lactide-co-glycolide) copolymer, and (c) a mixture of hydrophilic with lipophilic solvents, wherein said composition is effective to form a film encapsulated liquid *in situ*. First, Lewis disclose liquid compositions comprising 1 to 95% w% of a hydrophobic bioactive substance (see col 14 lines 5-10. also see example 1 lines 25-30.), (b) 1 to 75 w% of a poly(lactide-co-glycolide) copolymer, and (see claim 11.) (c) a mixture of hydrophilic with lipophilic solvents (see col 12.) Secondly, the newly amended limitation is in functional language and broadly indicate the ability of said composition to form (effective to form) a film encapsulated liquid *in situ*, which is an inherent property of the compositions disclosed by Lewis due to its similar formulation. In addition, it is Examiner's position that when solidification of a system such as one disclosed by Lewis begins, and the system forms a barrier wall on the outside of such polymer matrix, there is an amount of water that diffuse into the core of said polymeric system which remains within the formed sphere to constitute a gelatinous (semisolid)

composition. Further a gelatinous state, in accord to USP definition, constitutes small inorganic particles or large organic molecules interpenetrated by a liquid, wherein upon agitation will turn into liquid (see Remington: the science and practice of pharmacy 1995. Page 1517.) Therefore, Lewis's composition is effective to form a film encapsulated liquid *in situ*. Accordingly, claims 1-14 stand rejected.

6. Applicant's arguments filed on February 23, 2000 in respect to the rejection made under U.S.C. 103(a) as being unpatentable over Dunn et al US Patent 5,278,202, Yewey et al US Patent 5,780,044 and Lewis et al US Patent 5,733,566 has been considered, but were not found persuasive. First, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the general knowledge of the art indicate that the rate of precipitation of liquid polymeric compositions can be modified simply by changing the overall hydrophobicity/hydrophilicity of the copolymers. Second, both Lewis and Yewey teach that the physical parameters of the compositions cited in the prior art may be modified according to the polymer composition, polymer:drug ratio, and the size (see Lewis col 13 lines 1-19, and Yewey col 6 lines 13-30.) Dunn also indicates that the rate of coagulation or solidification may be

modified depending on the type of solvents selected (see col 5 lines 55-67.) Therefore one skilled in the art would have been able to select solvents that stay inside matrix for a longer period of time forming a film encapsulated liquid. Furthermore, the various concentrations of the bioactive drug, the copolymers, and the solvent mixture ration used in the instant compositions may be modified to best control the rate of releasing a drug of interest. Thirdly, the recitation of the independent claims use the open transitional language "comprising" which does not exclude the use of curing agents or any specific type of polymeric matrix. Finally, the broad recitation of the functional limitation "wherein said composition is effective to form a film encapsulated liquid in *situ*." does not exclude compositions that solidify *in situ,* because these composition inherently are effective to form a film encapsulated liquid as well. Accordingly, claims 1-14 stand rejected.

New Ground(s) of Rejection.

Applicant's amendments to the claims necessitated the new grounds of rejection because it has added a new limitation that directs the instant invention towards liquid polymeric compositions that are to form a film encapsulated liquid *in situ.*

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-14 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. The newly amended claim recites the functional limitation " wherein said composition is effective to form a film encapsulated liquid *in situ*." which is vague. It is not clear to what types of system is the applicant referring. Do the instant compositions maintain their polymeric system in liquid state or are they capable of retaining liquid inside the polymeric film wherein said film is to be formed *in situ*. One skilled in the art could not determine the specific meaning from the amount of knowledge provided in the instant disclosure. Therefore, the metes and bounds of the instant claims are not clear.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 1-14 rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Tipton et al US Patent 5,792,469.

The instant claims are directed to liquid polymeric compositions comprising a hydrophobic bioactive substance, a poly(lactide-co-glycolide) copolymer, and a mixture of hydrophilic with

lipophilic solvents, wherein said composition is effective to form a film encapsulated liquid *in situ.* The instant claims are also directed to methods of using said composition.

Tipton et al disclose liquid polymeric compositions comprising a hydrophobic bioactive substance such as fibroblast growth hormones, various antibacterial and antiparasitic agents (see col 9), suitable biocompatible polymers and copolymers such as polylactides and poly glycolides copolymers (see col 5 lines 8-24, claim 4), and solvents known in the art that have HLB ratios of about 9 to 13 (see col 6 lines 9-67), such as N-methyl-2-pyrrolidone, wherein said composition can solidify to form a gelatinous matrix or a film dressing (see col 12 lines 40-67.) It is Examiner's position that a gelatinous matrix as recognized by USP comprise a liquid matrix within, therefore, Tipton et al meet the limitations set forth in the instant claims.

Furthermore, although Tipton et al do not fully disclose a solvent mixture comprising a hydrophilic and lipophilic solvents, they indicate that their solvent system preferebly has an HLB value between 9 to 13 which is known in the art to make an oil in water solvent system, therefore, one ordinary skilled in the art would have been motivated to make Tipton's composition in a solvent mixture of hydrophilic and lipophilic solvents because making such system is well known in the art and Tipton et al have further indicated the characteristics of their preferred solvent system.

Conclusion

12. No claims were allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action, because addition of the new limitation has changed the

scope of the independent claims. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Jose Dees can be reached on 703-308-4628. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjs, 4/10/2000

SHELLEY A. DODSON
PRIMARY EXAMINER